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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/789,840	02/27/2004	Thomas J. Meade	068269-5002-US02	8243

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EXAMINER	
SAMALA, JAGADISHWAR RAO	
ART UNIT	PAPER NUMBER
1618	
MAIL DATE	DELIVERY MODE
02/02/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/789,840	MEADE, THOMAS J.	
	Examiner	Art Unit	
	JAGADISHWAR R. SAMALA	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 December 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,10-15 and 17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,10-15 & 17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of Applicant's Request for Continued Examination and Amendment filed on 12/10/2008.

Claims 1-4, 1—15 and 17 are pending in the instant application.

Claims 5-9 and 16 are withdrawn from consideration.

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/10/2008 has been entered.

Priority

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See Transco Products, Inc. v. Performance Contracting, Inc., 38 F.3d 551,32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. US 09/179,927 (now US 6,713,046), which claims benefit to US 60/063,328, fails to provide adequate

support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. Even though the US 60/063,328 document defines the enzyme targets as "enzymes associated with the generation or maintenance of arterioschlerotic plaques and lesions within the circulatory system, inflammation, wounds, immune response, and tumors, all tumors are basically not cancerous tumors. As such, the priority date for the full scope of instant claims was determined to be the filling date of the US 60/201,817 application, or 05.04./2000.

Claim Rejections - 35 USC § 102

2. Claims 1-4, 10-15 and 17 are rejected under 35 U.S.C. 102(e) as being anticipated by Snow et al. (US 5,932,188) is maintained for reasons of record in the previous office action filed on 06/11/2008.

Response to Arguments

Applicant argues that Snow reference does not anticipate the claims in part because it does not disclose the recited agents for their intended purpose. This argument is unpersuasive because, Snow does teach recited agents such as cytotoxic agent (means any agent able to kill cells, including radionuclide's, toxins, and chemotherapeutic agents such as cytotoxic drugs and cytotoxic antibiotics, or any agent that initiates or activates a host's immune response which leads to cell death (see col. 2 lines 43-48); chelating agent such as DOTA (col. 4 lines 35+); polymer that include both a therapeutic agent and moiety for enhancing contrast during MR imaging. For MR

imaging applications, the metal ion chelated by the chelator (M^{+a}) may include Cr^{+3}, Fe^{+3}, Gd^{+3} and Dy^{+3} (col. 8 lines 51+).

Applicant also argues that Snow reference does not teach the "off" MRI agent, would not be detectable and hence render those methods of diagnostic imaging unsuitable for their intended purpose. This argument is unpersuasive because claims does not recite that the MRI agent is initially "off" or "on" before administration. And more over Snow does teach that the polymer comprise both a therapeutic moiety and a moiety for enhancing contrast during x-rays or MR imaging that is suitable for intended purpose such as for the diagnostic imaging of tumors and the radiological treatment of tumors (col. 8 lines 51-55 and col. 10 lines 56-58).

Applicant also argues that Snow reference does not inherently disclose a chelator comprising a therapeutic blocking moiety. This argument is unpersuasive because Snow teaches composition comprising a therapeutic moiety (cytotoxic agents such as radionuclide's, antibiotics like doxorubicin, drugs selected form alkylating agents, antimetabolities, natural products, hormones and miscellaneous agents and a moiety for enhancing contrast during x-ray or MR imaging applications, (M^{+a}) may include Cr^{+3}, Fe^{+3}, Gd^{+3} and Dy^{+3} (col. 7 lines 31+ and col. 8 lines 51+). And also applicant's own admission of page 21(para 00111) of specification, recited a therapeutic blocking moiety can comprises a "therapeutically active agent" or "drug moiety" capable of causing a therapeutic effect, that is, it alters a biological function of a physiological target substance. Taking the information of the specification as a dictionary, the teaching of the reference anticipates that the composition has a capacity for interaction

with another component which may be found in biological fluids or associated with cells to be treated such as tumor cells. Thus, the teaching of the specification correlates with the prior art. Therefore, the applicant's argument is not persuasive regarding a therapeutic blocking moiety.

Thus, the Snow reference teaches either expressly or inherently impliedly, each and every limitation of the instant claims.

Claim Rejections – 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1-4, 10-15 and 17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-4, 10-15 and 17 are drawn to a method comprising: it is unclear what method applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 4 and 15 appears to contain a typographical error. The word " doxorubcin" should be corrected to "doxorubicin". Appropriate correction is required.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5. Claims 1-4, 10-15 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Meade et al (US 5,707,605) in view of Li et al (US 6,262,107 B1).

Applicant claims are drawn to a method comprising: administering an activatible MRI agent comprising chelator and a paramagnetic metal ion and a therapeutic blocking moiety covalently attached to said chelator, wherein said therapeutic blocking moiety comprises a cleavage site and an agent therapeutically active in cancer.

Meade et al discloses a resonance imaging agents (MRI agent) comprising a paramagnetic metal ion bound to a complex wherein said complex comprises a chelator and a blocking moiety covalently attached to said chelator, which binds in at least a fires coordination site of said metal ion and which is capable of interacting with a target substance such that the exchange of water in at least said first coordination site is increased (abstract). And preferred chelator is DOTA (col. 9 lines 49-65) and metal ions chelated by the chelator (M+)include Gd(III), Fe(III), Yt(III), Cr(III), and Dy(III) (col. 4 lines 31-35). And the MRI agent further comprises a blocking moiety which hinder the

rapid exchange of water in the remaining coordination site or sites, and which is capable of interacting with a target substance, which would read on substituted MRI agents (col. 4 lines 40, col. 5 line 1-30 and col. 6 lines 1-22). Additional disclosure includes that blocking moiety may comprise one or more linker groups to allow for correct spacing and attachment of the component of the blocking moiety. In one embodiment, blocking moieties include carbohydrate group which is capable of being cleaved by the carbohydrase enzyme (col. 15 lines 1-2). Further, the metal ion complexes have use as MRI contrast or enhancement agents to diagnose disease states of the brain, real –time detection and differentiation of myocardial infraction versus ischemia and may be used to perform rapid screens of the physiological response to drug therapy (col. 25 lines 1-7).

Meade meets claim limitation but fails to include therapeutic blocking moiety comprising an agent therapeutically active in cancer.

Li et al discloses a composition comprising a therapeutic agents, contrast agents and drugs including etopside, teniposide, doxorubicin, paclitaxel or docetaxel conjugated to a water soluble metal chelator (col. 2 lines 45+). And the drug paclitaxel is conjugated to a water soluble metal chelator such as DOTA wherein the metal ion chelator may be an ionic form of chromium, dysprosium, gadolinium, iron yttrium (col. 3 lines 62+ and col. 4 lines 12). Additional disclosure includes that the composition is used to treat of cancer, autoimmune diseases, restenosis and particularly the water soluble paclitaxel and docetaxel are each more effective than the other against certain

types of tumors, and those tumors that are more susceptible to a particular taxoid would be treated with that water soluble taxoid conjugate (col. 3 lines 56-61).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate a therapeutic agent/drug conjugated to a water soluble metal chelator into Meade MRI composition. The person of ordinary skill in the art would have been motivated to make these modification to prepare MRI composition comprising a therapeutic agent/drug conjugated to a water metal chelator and reasonably would have expected success, because water soluble paclitaxel and docetaxel composition as taught by Li can be used in same field of endeavor, such as for treatment of tumors, auto-immune disorders and for prediction of paclitaxel uptake by tumors and radiolabelled DOTA-paclitaxel tumor imaging.

Conclusion

1. No claims are allowed at this time.

2. Any inquiry concerning this communication or earlier communications from the examiner should be directed to JAGADISHWAR R. SAMALA whose telephone number is (571)272-9927. The examiner can normally be reached on 8.30 A.M to 5.00 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571)272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jake M. Vu/
Primary Examiner, Art Unit 1618

Jagadishwar R Samala
Examiner
Art Unit 1618

sjr